

**REMARKS****I. Status of the Claims**

Claims 1-9, 15 and 18-37 were pending in this application at the time of the Office Action dated January 29, 2007. Claims 1-6, 8, 9, 15, 28-33 and 35 were under examination and claims 7, 18-27, 34, 36 and 37 were withdrawn from consideration. As a result of this amendment, new claims 38 and 39 have been added. Accordingly, claims 1-6, 8, 9, 15, 28-33, 35, 38 and 39 are now pending and under examination.

**II. Amendments to the Specification and the Claims**

Claim 1 has been amended above to more clearly define the invention. Specifically, claim 1 has been amended to delete superfluous language, and to refer to a method for optimizing the production of monoclonal antibodies that bind to cell surface antigens wherein the population of antibodies thereby produced contains fewer non-representative monoclonal antibodies that bind to proteins not present on said particular cell type and more monoclonal antibodies that bind to intact cell surface antigens of said particular cell type as compared to a similarly sized population of different monoclonal antibodies generated from a like host mammal immunized with a plurality of like viable and intact cells whose surfaces are not free of serum. Support for this amendment may be found throughout the specification, for example at page 2, lines 1-4; page 3, lines 2-7, page 16, lines 10-28 and the abstract.

In addition, new claims 38-40 have been added. Claim 38 is dependent on claim 1 and recites that the host mammal is immunized by intraperitoneal injection. Support for this claim may be found at the very least at page 15, lines 7-8. Claim 39 is also dependent on claim 1 and recites

that the method comprises generating a population of antibody-producing hybridoma clones from said immunized mammal. Support for this claim may be found throughout the specification, for instance at page 4, lines 13-22.

### **III. Species Election**

Claims 34, 36 and 37 have been withdrawn from further consideration because of Applicants' species election. Applicants respectfully submit that the claimed methods are not limited to a particular cell type. Applicants respectfully request that the withdrawn species be examined and included upon allowance of a generic claim.

### **IV. Rejections Under 35 U.S.C. §103(a)**

Claims 1-6, 8, 9, 15, 28-33 and 35 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Okabe et al. in view of US 5,364,785 as evidenced by US 5,932,704. Although the Examiner acknowledges that Okabe et al. fails to teach a method of producing antibodies using intact cells in the absence of serum, the Examiner apparently believes it would have been obvious to use the serum free cells of US 5,932,704 to generate antibodies using the method of Okabe et al. Applicants respectfully traverse the rejection, particularly in light of the amendments to claim 1 above.

Claim 1 has been amended above to clarify that the methods of the invention provide a method of optimizing antibody production following immunization whereby the production of non-representative monoclonal antibodies that bind to proteins not present on the cell type of interest is minimized and the production of monoclonal antibodies that bind to intact cell surface antigens of

the cell type of interest is maximized. Applicants have surprisingly found that immunizing a suitable mammalian host with intact and viable cells that are also serum free results in an unforeseen enhancement in the production of relevant monoclonal antibodies that would not have been obvious to the skilled artisan in light of the prior art at the time of filing.

For example, as shown in the attached 1.132 declaration by inventor Jennie P. Mather, four times more positive hybridoma clones were found to produce monoclonal antibodies directed to surface antigens when serum-free cells were employed as immunogens and injected intraperitonealy. As shown in Table 1 of the declaration, 12% of the hybridomas obtained from the mice injected with serum-free cells produced monoclonal antibodies exhibiting specific binding to intact cells whereas only 3% of the hybridomas generated from the mice immunized with serum-cultured cells secreted monoclonal antibodies reactive with intact cells. Further, while foot-pad immunization also resulted in an increase of relevant monoclonal antibodies when performed with serum-free cells, intraperitoneal injection of cells was about twice as effective.

According to the Federal Circuit, "[a] greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness ... of the claims at issue." *In re Corkill*, 711 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985). Here, a four-fold increase in the retrieval of relevant cell surface specific monoclonal antibodies is much higher than one would have expected and provides a significant, practical advantage for those developing antibodies toward cell surface targets via whole cell immunization.

In light of the above amendments and remarks and also the 132 declaration submitted herewith, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

This reply is fully responsive to the Office Action dated January 29, 2007. Therefore, a Notice of Allowance is next in order and is respectfully requested.

If the Examiner has any further questions relating to this Reply or to the application in general, she is respectfully requested to contact the undersigned by telephone so that allowance of the present application may be expedited. Applicants would appreciate a telephonic interview with the Examiner prior to further examination.

**CONCLUSION**

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 415072000101. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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